<110> Bledsoe, Randy, K

     Lambert, Millard, H

     Montana, Valerie, G

     Stewart, Eugene, L

     Xu, H., Eric

<120> STRUCTURE OF A GLUCOCORTICOID RECEPTOR LIGAND BINDING DOMAIN
COMPRISING AND EXPANDED BINDING POCKET AND METHODS EMPLOYING SAME

<130> PU4803

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<170> PatentIn version 3.1

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Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
                20                  25                  30
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     Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
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15   ttt cca aaa ggc tca gta agc aat gcg cag cag cca gat ctg tcc aaa    240
     Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
     65              70                  75                  80

     gca gtt tca ctc tca atg gga ctg tat atg gga gag aca gaa aca aaa    288
     Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
                     85                  90                  95

20   gtg atg gga aat gac ctg gga ttc cca cag cag ggc caa atc agc ctt    336
     Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
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25   tcc tcg ggg gaa aca gac tta aag ctt ttg gaa gaa agc att gca aac    384
     Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
             115                 120                 125

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     Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
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    Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
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    Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
    305             310             315             320

    gtt cat ggt gtg agt acc tct gga gga cag atg tac cac tat gac atg    1008
    Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
                    325             330             335

    aat aca gca tcc ctt tct caa cag cag gat cag aag cct att ttt aat    1056
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    Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
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    cct ccc aaa ctc tgc ctg gtg tgc tct gat gaa gct tca gga tgt cat    1296
    Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
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    Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
    465             470             475             480

    tgt ctt cag gct gga atg aac ctg gaa gct cga aaa aca aag aaa aaa    1488
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                485             490             495

    ata aaa gga att cag cag gcc act aca gga gtc tca caa gaa acc tct    1536
    Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
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                            565             570             575

            tgg gca aag gca ata cca ggt ttc agg aac tta cac ctg gat gac caa    1776
            Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln
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    45                      675             680             685

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            tta gct gaa atc atc acc aat cag ata cca aaa tat tca aat gga aat    2304
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Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
            100                 105                 110

Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
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Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
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        Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
        225             230             235             240
15      Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
                    245             250             255

20      Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
                    260             265             270

        Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
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        Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
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        Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
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        Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
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 10     465                    470                    475                    480

        Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
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        Met Thr Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Ala Phe Ala Leu
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        Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala
            610                    615                    620
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        Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr
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        Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu
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        Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
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     Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
                 740             745             750
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     1               5               10              15
45
     agt gtg ctt gct cag gag agg gga gat gtg atg gac ttc tat aaa acc     96
     Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
                 20              25              30

50   cta aga gga gga gct act gtg aag gtt tct gcg tct tca ccc tca ctg    144
     Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu
                 35              40              45

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             50              55              60

     ttt cca aaa ggc tca gta agc aat gcg cag cag cca gat ctg tcc aaa    240
     Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
60   65              70              75              80

     gca gtt tca ctc tca atg gga ctg tat atg gga gag aca gaa aca aaa    288
     Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
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                        85                      90                      95

      gtg atg gga aat gac ctg gga ttc cca cag cag ggc caa atc agc ctt         336
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      tcc tcg ggg gaa aca gac tta aag ctt ttg gaa gaa agc att gca aac         384
      Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
 10                   115                 120                 125

      ctc aat agg tcg acc agt gtt cca gag aac ccc aag agt tca gca tcc         432
      Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
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 15   act gct gtg tct gct gcc ccc aca gag aag gag ttt cca aaa act cac         480
      Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
      145                 150                 155                 160

 20   tct gat gta tct tca gaa cag caa cat ttg aag ggc cag act ggc acc         528
      Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
                          165                 170                 175

 25   aac ggt ggc aat gtg aaa ttg tat acc aca gac caa agc acc ttt gac         576
      Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp
                      180                 185                 190

      att ttg cag gat ttg gag ttt tct tct ggg tcc cca ggt aaa gag acg         624
 30   Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr
                      195                 200                 205

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      Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
 35                   210                 215                 220

      ctt tct cct ctg gcg gga gaa gac gat tca ttc ctt ttg gaa gga aac         720
      Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
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                          245                 250                 255

 45   att aag gat aat gga gat ctg gtt ttg tca agc ccc agt aat gta aca         816
      Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
                      260                 265                 270

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 50   Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
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 55                   290                 295                 300

      agc ttt cct gga gca aat ata att ggt aat aaa atg tct gcc att tct         960
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 60   gtt cat ggt gtg agt acc tct gga gga cag atg tac cac tat gac atg         1008
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                          325                 330                 335
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aat aca gca tcc ctt tct caa cag cag gat cag aag cct att ttt aat    1056
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            340             345                 350

gtc att cca cca att ccc gtt ggt tcc gaa aat tgg aat agg tgc caa    1104
Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
            355             360                 365

gga tct gga gat gac aac ttg act tct ctg ggg act ctg aac ttc cct    1152
Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
            370             375                 380

ggt cga aca gtt ttt tct aat ggc tat tca agc ccc agc atg aga cca    1200
Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
385             390                 395                 400

gat gta agc tct cct cca tcc agc tcc tca aca gca aca aca gga cca    1248
Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro
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cct ccc aaa ctc tgc ctg gtg tgc tct gat gaa gct tca gga tgt cat    1296
Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
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tat gga gtc tta act tgt gga agc tgt aaa gtt ttc ttc aaa aga gca    1344
Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
            435             440                 445

gtg gaa gga cag cac aat tac cta tgt gct gga agg aat gat tgc atc    1392
Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile
    450             455                 460

atc gat aaa att cga aga aaa aac tgc cca gca tgc cgc tat cga aaa    1440
Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
465             470             475                 480

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Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
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Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
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gaa aat cct ggt aac aaa aca ata gtt cct gca acg tta cca caa ctc    1584
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acc cct acc ctg gtg tca ctg ttg gag gtt att gaa cct gaa gtg tta    1632
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545             550             555                 560

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                     660             665                 670

         tct tca gtt cct aag gac ggt ctg aag agc caa gag cta ttt gat gaa      2064
   25    Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu
                     675             680                 685


   30    att aga atg acc tac atc aaa gag cta gga aaa gcc att gtc aag agg      2112
         Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
                 690             695                 700

         gaa gga aac tcc agc cag aac tgg cag cgg ttt tat caa ctg aca aaa      2160
   35    Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys
         705             710                 715                 720

         ctc ttg gat tct atg cat gaa gtg gtt gaa aat ctc ctt aac tat tgc      2208
         Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys
   40                725                 730                 735

         ttc caa aca ttt ttg gat aag acc atg agt att gaa ttc ccc gag atg      2256
         Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
                     740                 745                 750
   45
         tta gct gaa atc atc acc aat cag ata cca aaa tat tca aat gga aat      2304
         Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn
                 755                 760                 765

   50    atc aaa aaa ctt ctg ttt cat caa aag tga                            2334
         Ile Lys Lys Leu Leu Phe His Gln Lys
             770                 775


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         <213>  Homo sapiens
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10   Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr
                 20              25                  30


     Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu
15           35              40                  45


     Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp
         50              55                  60
20

     Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys
     65              70                  75              80


25   Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys
                 85                  90                  95


     Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu
30               100                 105                 110


     Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn
35           115                 120                 125


     Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser
         130                 135                 140
40

     Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His
     145                 150                 155                 160
45

     Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr
                 165                 170                 175


50   Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp
                 180                 185                 190


55   Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr
             195                 200                 205


     Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu
         210                 215                 220
60

     Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn
     225                 230                 235                 240
```

```
      Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys
 5                245                 250                 255

      Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr
                      260                 265                 270
10
      Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr
                  275                 280                 285
15
      Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala
              290                 295                 300

      Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser
20    305                 310                 315                 320

      Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met
                      325                 330                 335
25
      Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn
                  340                 345                 350
30
      Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln
              355                 360                 365

35    Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro
          370                 375                 380
      Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro
      385                 390                 395                 400
40
      Asp Val Ser Ser Pro Pro Ser Ser Ser Thr Ala Thr Thr Gly Pro
                      405                 410                 415

45    Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His
                  420                 425                 430

      Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala
50            435                 440                 445

      Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile
          450                 455                 460
55
      Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
      465                 470                 475                 480
60
      Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys Lys
                      485                 490                 495
```

```
      Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser
                  500                 505                 510
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      Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu
                  515                 520                 525
10    Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu
                  530                 535                 540
      Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met
15    545                 550                 555                 560
      Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys
                      565                 570                 575
20
      Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln
                  580                 585                 590
25
      Met Thr Leu Leu Gln Tyr Ser Trp Met Ser Leu Met Ala Phe Ala Leu
                  595                 600                 605
30    Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala
                  610                 615                 620
      Pro Asp Leu Ile Ile Asn Glu Gln Arg Met Thr Leu Pro Cys Met Tyr
35    625                 630                 635                 640
      Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu
                      645                 650                 655
40    Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu
                  660                 665                 670
      Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu
45                675                 680                 685
      Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
                  690                 695                 700
50
      Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys
      705                 710                 715                 720
55
      Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys
                      725                 730                 735
60    Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met
                  740                 745                 750
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            Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn
                    755                 760                 765
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            Ile Lys Lys Leu Leu Phe His Gln Lys
                770                 775
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            <222>  (1)..(771)
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            Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Leu Leu
            1               5                   10                  15
```

35
```
            gag gtt att gaa cct gaa gtg tta tat gca gga tat gat agc tct gtt      96
            Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
                        20                  25                  30
```

40
```
            cca gac tca act tgg agg atc atg act acg ctc aac atg tta gga ggg     144
            Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
                    35                  40                  45
```

45
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            cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc     192
            Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
                50                  55                  60
```

50
```
            agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg     240
            Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
            65                  70                  75                  80
```

```
            atg ttt ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca     288
            Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
                            85                  90                  95
```

55
```
            agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag     336
            Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
                            100                 105                 110
```

60
```
            aga atg act cta ccc tgc atg tac gac caa tgt aaa cac atg ctg tat     384
            Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
                        115                 120                 125
```

```
            gtt tcc tct gag tta cac agg ctt cag gta tct tat gaa gag tat ctc     432
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```
       Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
           130             135             140

  5    tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg      480
       Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
       145             150             155             160

       aag agc caa gag cta ttt gat gaa att aga atg acc tac atc aaa gag      528
       Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 10                    165             170             175

       cta gga aaa gcc att gtc aag agg gaa gga aac tcc agc cag aac tgg      576
       Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
                   180             185             190
 15
       cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg      624
       Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
                   195             200             205

 20    gtt gaa aat ctc ctt aac tat tgc ttc caa aca ttt ttg gat aag acc      672
       Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
           210             215             220

       atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag      720
       Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 25    225             230             235             240

       ata cca aaa tat tca aat gga aat atc aaa aaa ctt ctg ttt cat caa      768
       Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
 30                    245             250             255

       aag tga                                                              774
       Lys
 35

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       <213>   Homo sapiens

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       Val Pro Ala Thr Leu Pro Gln Leu Thr Pro Thr Leu Val Ser Leu Leu
       1               5               10                      15
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       Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
                   20              25              30

 55    Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
                   35              40              45


       Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
 60        50              55              60


       Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
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-17-

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            65                      70                      75                      80

  5    Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
                         85              90              95


       Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
 10                  100             105             110


       Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
                   115             120             125
 15
       Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
                   130             135             140

 20    Cys Met Lys Thr Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
       145             150             155             160


       Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 25                  165             170             175


       Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
                   180             185             190
 30
       Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
                   195             200             205

 35
       Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
                   210             215             220


 40    Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
       225             230             235             240


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1           5               10              15

gag gtt att gaa cct gaa gtg tta tat gca gga tat gat agc tct gtt     96
Glu Val Ile Glu Pro Glu Val Leu Tyr Ala Gly Tyr Asp Ser Ser Val
            20              25              30

cca gac tca act tgg agg atc atg act acg ctc aac atg tta gga ggg    144
Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
        35              40              45

cgg caa gtg att gca gca gtg aaa tgg gca aag gca ata cca ggt ttc    192
Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
    50              55              60

agg aac tta cac ctg gat gac caa atg acc cta ctg cag tac tcc tgg    240
Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
65              70              75              80

atg tcc ctt atg gca ttt gct ctg ggg tgg aga tca tat aga caa tca    288
Met Ser Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
                85              90              95

agt gca aac ctg ctg tgt ttt gct cct gat ctg att att aat gag cag    336
Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
            100             105             110

aga atg act cta ccc tgc atg tac gac caa tgt aaa cac atg ctg tat    384
Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
            115             120             125

gtt tcc tct gag tta cac agg ctt cag gta tct tat gaa gag tat ctc    432
Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
    130             135             140

tgt atg aaa acc tta ctg ctt ctc tct tca gtt cct aag gac ggt ctg    480
Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
145             150             155             160

aag agc caa gag cta ttt gat gaa att aga atg acc tac atc aaa gag    528
Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
                165             170             175

cta gga aaa gcc att gtc aag agg gaa gga aac tcc agc cag aac tgg    576
Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
            180             185             190

cag cgg ttt tat caa ctg aca aaa ctc ttg gat tct atg cat gaa gtg    624
Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
            195             200             205
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gtt gaa aat ctc ctt aac tat tgc ttc caa aca ttt ttg gat aag acc        672
Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
    210             215             220

atg agt att gaa ttc ccc gag atg tta gct gaa atc atc acc aat cag        720
Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
225             230             235             240

ata cca aaa tat tca aat gga aat atc aaa aaa ctt ctg ttt cat caa        768
Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
                245             250             255

aag tga                                                                774
Lys
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<212> PRT

<213> Homo sapiens

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            20              25              30

Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly
        35              40              45

Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe
    50              55              60

Arg Asn Leu His Leu Asp Asp Gln Met Thr Leu Leu Gln Tyr Ser Trp
65              70              75              80

Met Ser Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser
            85              90              95

Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asn Glu Gln
            100             105             110

Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr
            115             120             125

Val Ser Ser Glu Leu His Arg Leu Gln Val Ser Tyr Glu Glu Tyr Leu
```

```
           130                    135                    140

     Cys Met Lys Thr Leu Leu Leu Leu Ser Ser Val Pro Lys Asp Gly Leu
  5  145                150                155                    160

     Lys Ser Gln Glu Leu Phe Asp Glu Ile Arg Met Thr Tyr Ile Lys Glu
 10                     165                170                175

     Leu Gly Lys Ala Ile Val Lys Arg Glu Gly Asn Ser Ser Gln Asn Trp
                       180                185                190
 15

     Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val
                   195                200                205
 20  Val Glu Asn Leu Leu Asn Tyr Cys Phe Gln Thr Phe Leu Asp Lys Thr
                   210                215                220

     Met Ser Ile Glu Phe Pro Glu Met Leu Ala Glu Ile Ile Thr Asn Gln
 25  225                230                235                    240

     Ile Pro Lys Tyr Ser Asn Gly Asn Ile Lys Lys Leu Leu Phe His Gln
                       245                250                255
 30
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Leu Leu Arg Tyr Leu Leu
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30